AWARD NUMBER: W81XWH-16-2-0021

TITLE: A novel vector control measure to combat the spread of artemisinin resistance in the Greater Mekong Subregion

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14. ABSTRACT

Survey for study site selection was conducted in 4 provinces, in Thailand; Ranong, Surat Thani, Ratchaburi and Kanchanaburi. Blood was collected by finger pricking from population at selected sites. Blood samples from people with malaria symptom were examined for malaria by RDT on site. Malaria examination by quantitative PCR or qMal was performed for all samples. More than 5,100 blood samples were collected, among this 346 of them had symptom during the survey. There were 35 samples positive for malaria by qMal and 4 samples were positive by RDT. Preliminary entomology surveys were conducted during reporting period for planning purpose for the vector survey which will be started in FY2018. Database management system has been established for the study including, but not limited to, blood survey forms, GIS mapping of sites, etc. Laboratory protocols have been validated and applied for blood survey and will be used for vector survey. Protocols for longitudinal blood survey and vector survey have been prepared and submitted for HRPO pre-review. Sites in Surat Thani will selected for the further longitudinal study based on recent analysis. Longitudinal surveillance will be conducted in FY2018 prior to ivermectin mass drug administration to ensure that there will be enough population with malaria for randomized controlled trial.

15. SUBJECT TERMS
Malaria, transmission, ivermectin, mass drug administration, elimination, vector control

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	21	19b. TELEPHONE NUMBER (include area code)

TABLE OF CONTENTS

1. **INTRODUCTION**: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Novel vector control tools are urgently needed to aid malaria elimination and artemisinin containment efforts in the Greater Mekong Subregion (GMS). Globally, ivermectin is lethal to all Anopheles vectors of malaria tested to date. Ivermectin mass drug administration (MDA) has been shown to suppress both mosquito and human parameters of malaria parasite transmission in West Africa. We will investigate whether ivermectin MDA to people in Thailand can reduce Plasmodium transmission. We will select several villages in southern Thailand and monitor both mosquito (parity rate, sporozoite rate) and human (malaria prevalence, malaria incidence) parameters of malaria transmission before, during, and after ivermectin MDAs in control and treated villages. If successful, then ivermectin MDA has the potential to become a new vector control tool to suppress Plasmodium transmission and accelerate malaria elimination efforts in the GMS.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Ivermectin, mass drug administration, human, malaria, ***Plasmodium***, prevalence, transmission, vector control, ***Anopheles dirus***, ***Anopheles minimus***, parity, Thailand

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.
What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Major Task 1: Prepare field site for study initiation
Subtask 1: Prepare Regulatory Documents and Research Protocol for Blood and Mosquito Collection

- CRADAs finalized for: Mahidol-CDMRP (30 Sep 2016), Mahidol-Geneva (22 Sep 2016), Geneva-WRAIR/AFRIMS (9 Mar 2017), Mahidol-AFRIMS (19 Jul 2017).
- Coordinate with sites for human use protocol submissions:

1) Cross-sectional blood survey for site selection protocol: approved (7 Jun 2017 from Faculty of Tropical Medicine Ethics Committee; 28 Jun 2017 from Ministry of Public Health Ethics Committee; 20 Jul 2017 from HRPO)
2) Longitudinal blood survey for site evaluation protocol: drafted, submission pending (Nov 2017)
3) Mosquito collection for site evaluation protocol: drafted, submitted Thai MoPH twice, third submission pending HRPO pre-review (Oct 2017)

- Coordinate with Sites for job descriptions, interview, hire staff – completed
- Dr. Kevin Kobylinski was hired by the Geneva Foundation (17 Apr 2017)
- Two Entomology staff (one postdoc, one technician) hired by Mahidol University will assist Dr. Kobylinski in vector surveillance.
- Coordinate with sites for training

1) Cross-sectional blood surveys, all Mahidol and local public health staff trained (15 May 2017, 6 Jul 2017, 19-20 Jul 2017).
2) Entomology team site visit (24-30 Jul 2017), coordinated with local public health staff to validate capacity to support entomology objectives – training of local persons to support human landing collections will commence once human use protocol is approved

Subtask 2: Establish logistics at field site

- Coordinate with Thai MoPH, border patrol, and malaria clinics to identify participant villages – completed
  - Conduct small focus groups with Village Chiefs, Rubber Plantation Owners, and Village Health Volunteers to obtain permission to work in area
    - Key Personnel met with Dr. Siriluck Thaicharoen, Director of Region 11 Office of Prevention and Disease Control, Department of Disease Control, and obtained permission to perform study (9 May 2017)
    - Small group discussions with Village Chiefs and Village Health Volunteers to prepare study area have been initiated (Jul – Aug, 2017), pending human use protocols for full discussions.
  - Conduct town hall meetings to explain study to local residents
    - Study was explained to local residents of the study sites during their monthly town hall meetings in prior to blood collection.
  - Obtain consent from local residents – completed for cross-sectional blood surveys, pending human use protocol approvals for longitudinal blood collection surveys, mosquito surveys, ivermectin MDAs
    - Identify and train local residents to assist blood and mosquito collections – pending human use protocol approvals
    - Conduct GIS and demographic surveys – completed initial village level mapping, detailed household level mapping and demographic surveys pending longitudinal blood survey protocol approval
    - Construct barrier screens and HLC shelters – pending mosquito collection human use protocol approval

Major Task 2: Initiate blood and mosquito collections

Subtask 1: Facilitate Blood Collections and Social Science at field site

- Cross-sectional surveys were conducted in four areas. Plasmodium prevalence in each area was determined to assist in site selection for MDA.
- Social science questionnaires have been prepared– preliminary demographics were collected during the cross-sectional survey, however full scale questionnaires will be performed after longitudinal blood survey protocol is approved.

Subtask 2: Facilitate Mosquito Collections via Human Landing Collections (HLC)

- Preliminary mosquito survey was performed 24-30 Jul 2017 using CDC light traps. Full scale mosquito collection efforts are pending human use protocol approval.

Major Task 3: Prepare and Initiate Ivermectin MDAs

- This task will be initiated in FY2019

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) Major Activities:

- Key Investigators made field site visits to Surat Thani (27 Oct 2016) and Ranong (3 Nov 2016) to meet with local MoPH staff to discuss study, logistics, and barriers to project implementation

- GIS team visited Surat Thani and Ranong (21-25 Nov 2016) to perform preliminary mapping of villages and prior malaria cases (2015-2017) to help select target areas for cross-sectional surveys
- Key Investigators made field site visit to Surat Thani (11 May 2017) to discuss project logistics of cross-sectional blood survey with local MoPH staff
- Entomology team visited Surat Thani (24-30 Jul 2017) to observe local MoPH staff perform human landing collections to ensure field techniques, logistics, resources and supplies are compatible with Entomology objectives.
- Cross-sectional blood survey was completed in Ranong (7 -12 Aug 2017), Surat Thani (14-18 Aug 2017), Kanchanburi (28 Jul – 1 Aug 2017), and Ratchaburi (22 Aug -28 Aug 2017), molecular analyses completed on 30 Sep 2017.
- Molecular tools required for vector and malaria survey were evaluated and validated.

2) Specific Objectives:

- Survey to select the proper sites for ivermectin MDA.
- Validation of laboratory protocols for parasites and vector survey.

3) Significant Results:

- Total of 5177 blood samples were collected, only 5155 samples were tested for malaria by qMal. There were 346 people had malaria related symptom during blood collection thus RDT for malaria was used on site to confirm if they had malaria infection. There were 4 RDT positive among these symptomatic. Summary of blood survey and malaria examination for each site was shown in Appendic section.
- Cross-sectional blood survey results indicated that Surat Thani is the most promising field site to perform the ivermectin MDAs. Of the four provinces surveyed, Surat Thani had the highest Plasmodium positive prevalence by qMal and all identified *Plasmodium* infection were due to *P. falciparum* which is the ideal parasite to evaluate during ivermectin MDAs.
- Preliminary entomology surveys and discussion with MoPH staff confirm that both *An. minimus* and *An. dirus* are present at the study area and *An. minimus* is most likely responsible for most of the malaria transmission. This means that it will be possible to evaluate the impact of ivermectin MDAs on *An. minimus* parity rates as planned.
- Entomology mosquito group (*An. dirus*, *An. minimus*, *An. maculatus*) species identification via PCR validated, detection of *Plasmodium* in *Anopheles* via RT-PCR validated. *Plasmodium falciparum*-infected *An. dirus* for use as positive controls were kindly provided by a colleague at the NIH, Dr. Alvaro Molina-Cruz. Mosquito field samples caught via light traps in Surat Thani during training visit were successfully characterized molecularly to species.

4) Other Achievements:

What opportunities for training and professional development has the project provided?

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

- Dr. Kevin Kobylinski (Co-PI) was an invited speaker and presented on the use of ivermectin mass drug administration for malaria elimination at the "International Conference on *Plasmodium Vivax* Research", 11-14 Jun 2017, Manaus Brazil. No CDMRP funds were used to support this travel.
- Entomology team visited Surat Thani (24-30 Jul 2017) to observe local MoPH staff perform human landing collections and train Entomology staff to ensure field techniques, logistics, resources and supplies are compatible with Entomology objectives.
- Entomology team trained twice with Yudthana Samung, an expert entomologist at Mahidol University, to validate our competency for mosquito ovary dissections and evaluation of parity status.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

- During the initial cross-sectional blood survey for site selection the community was engaged by the blood collection team to educate the local community on the importance of malaria transmission in their communities.
- The results of plasmodium detection by qMal from the site-selection survey were reported back to the Offices of Disease Prevention and Control (No. 5 &11) which oversees the malaria control activities in the study sites.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."
Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

- Once longitudinal blood survey and mosquito survey protocols are approved by the Thai MoPH, then we will return to Surat Thani and engage the local community to explain the importance of the study by holding small group discussions with key community leaders including MoPH staff, Village Chiefs, Rubber plantation owners, Village Health Volunteers, and then town hall meetings with the entire community.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:
What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

The cross-sectional malaria survey provided an update on malaria infection status in four at-risk provinces in Thailand. This information allowed us to select the ideal field site for the ivermectin MDA study and may be useful information for future studies or surveys.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- transfer of results to entities in government or industry;
- instances where the research has led to the initiation of a start-up company; or
- adoption of new practices.

Nothing to Report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- improving public knowledge, attitudes, skills, and abilities;
- changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or
- improving social, economic, civic, or environmental conditions.

Nothing to Report

5. **CHANGES/PROBLEMS**: The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Due to the sharp decline in malaria prevalence in Thailand in the last three years, the malaria prevalence at the field site is much reduced compared to projections in the grant. Therefore, we felt it necessary to survey four potential sites to ensure that we selected the ideal field site to perform and evaluate ivermectin MDAs. The reduced malaria prevalence means that we will have to sample more people during blood surveys and treat more people during ivermectin MDAs in order to demonstrate a significant drop in malaria prevalence and incidence. Increased costs for blood surveys and ivermectin treatment can be offset by performing fewer blood surveys per year and or reducing the number of blood surveys in year four of post intervention follow up. The investigators still plan to complete the project within the awarded budget.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

There were delays in local MoPH EC approval for the cross-sectional blood survey and the mosquito collection protocol is still under review. We are in the process of responding to IRB inquiries for the mosquito collection protocol and we hope to have longitudinal blood surveys submitted soon.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Delays in human use approvals have pushed back expenditures. This will be rectified in the coming year when ethical approvals are in place and full scale blood and mosquito sampling commences. The reduced malaria prevalence means that we will have to sample more people during blood surveys and treat more people during ivermectin MDAs in order to demonstrate a significant drop in malaria prevalence and incidence. Increased costs for blood surveys and ivermectin treatment can be offset by performing fewer blood surveys per year and or reducing the number of blood surveys in year four of post intervention follow up. The investigators still plan to complete the project with the awarded budget.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.
Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Not Applicable

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- Publications, conference papers, and presentations
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

  Nothing to Report

  Books or other non-periodical, one-time publications. Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

Nothing to Report

Other publications, conference papers, and presentations. Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Nothing to report

- **Website(s) or other Internet site(s)**
List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

MESA
http://www.malariaeradication.org/mesa-track/novel-vector-control-measure-combat-spread-artemisinin-resistance-greater-mekong

- **Technologies or techniques**
Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**
Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **Other Products**
  - Identify any other reportable outcomes that were developed under this project.

Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life.

- **Biospecimen collections: blood samples were collected from cross-sectional survey for plasmodium detection. Purified blood DNA and plasma samples have been archived and will be kept until the end of the study.**

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Mahidol University Key Personnel

Name:	Jetsumon Prachumsri
Project Role:	Principal Investigator (PI) of Project
Nearest Person Month Worked:	3
Contribution to Project:	Overall coordination of the study, preparing progress reports, overseeing the direction of the study, and overseeing laboratory personnel

Name:	Pratap Singhasivanon
Project Role:	Blood Surveillance/MDA Coordinator
Nearest Person Month Worked:	1
Contribution to Project:	Project leader for blood surveillance and mass drug administration (MDA) coordinator

Name:	Jeeraphat Sirichaisinthop
Project Role:	Ministry of Public Health Coordinator
Nearest Person Month Worked:	1
Contribution to Project:	Oversee that all tasks performed with the endemic population are reported to the Thai Ministry of Public Health correctly. Co-PI on the study human use protocol.

Name:	Jaranit Kaewkungwal
Project Role:	Data Management Coordinator
Nearest Person Month Worked:	2
Contribution to Project:	Managing all data produced from the study

Name:	Wang Nguitragool
Project Role:	Molecular Analysis Team Leader
Nearest Person Month Worked:	4
Contribution to Project:	Leading the team involved in molecular analysis of blood samples collected during the study

Name:	Suparat Phuanukoonnon
Project Role:	Social Science Co-ordinator
Nearest Person Month Worked:	1
Contribution to Project:	Responsible for site preparation, coordinating meeting community leaders to inform them about the proposed study and design and manage the social science study part of the proposed study.

Mahidol University: Project Administration

Name:	Pornpimon Adams
Project Role:	Project Coordinator/Admin. Manager
Nearest Person Month Worked:	2
Contribution to Project:	Overall coordination/management of administrative, legal, financial, compliance, reporting, and logistics of project sites.

Name:	Paul Adams
Project Role:	Research Administrator
Nearest Person Month Worked:	6
Contribution to Project:	Research administration: oversight, supervision and performance of administrative, legal, financial, compliance, reporting, etc. roles.

Geneva Foundation/AFRIMS/WRAIR

Name:	Kevin Kobylinski
Project Role:	Subaward Principal Investigator
Nearest Person Month Worked:	12
Contribution to Project:	Principal Investigator for The Geneva Foundation and oversees all work conducted at AFRIMS.

Name:	Ratree Takhampunya
Project Role:	Co-Investigator
Nearest Person Month Worked:	1
Contribution to Project:	Dr. Takhampunya is the Chief of the AFRIMS Department of Entomology Diagnostics and Re-Emerging Diseases section. She provides oversight of all aspects of molecular mosquito processing.

Name:	Maj. Silas Davidson
Project Role:	Co-investigator
Nearest Person Month Worked:	1
Contribution to Project:	Maj. Davidson is Chief of the AFRIMS Department of Entomology. He provides oversight of all administrative and human subjects issues pertaining to the project.

Name:	Maj. Wes McCardle
Project Role:	Co-Investigator
Nearest Person Month Worked:	1
Contribution to Project:	Maj. McCardle is the Chief of the WRAIR Entomology Branch Department of Vector and Parasite Biology. He provides statistical expertise and support on the project.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

If there is nothing significant to report during this reporting period, state "Nothing to Report."
If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."
Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- Financial support;
- In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);
- Facilities (e.g., project staff use the partner's facilities for project activities);
- Collaboration (e.g., partner's staff work with project staff on the project);
- Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and
- Other.

1. **Subaward: The Geneva Foundation, provides grants management support.**
Subaward Performance Site: Armed Forces Research Institute of Medical Sciences (AFRIMS), located in Bangkok, Thailand.
- **Collaboration**
- **Facilities**

8. SPECIAL REPORTING REQUIREMENTS: QUAD CHARTS

A novel vector control measure to combat the spread of artemisinin resistance in the Greater Mekong Subregion
Log Number: PR150881
Award Number: W81XWH-16-2-0021
Annual Report 29 October 2017

PI: Dr. Jetsumon Prachumsri **Org:** Mahidol University **Award Amount: $6,973,329.00**

Study Aim

- Evaluate efficacy of ivermectin (study 1) mass drug administration to humans to reduce both entomological and epidemiological parameters of malaria transmission
- Evaluate efficacy of multi-drug (study 2) mass drug administration to humans to reduce both entomological and epidemiological parameters of malaria transmission

Approach

- Perform longitudinal collections of blood samples for *Plasmodium* detection by molecular analysis
- Perform longitudinal collections of mosquito samples to determine age structure by dissection and species identification and *Plasmodium* detection by molecular analysis
- Perform mass drug administrations and assess effects on epidemiological and entomological transmission parameters

Cross-sectional mass blood survey during July 28-Aug 28, 2017. Plasmodium prevalence at 4 sites (left) and blood collection station (right).

Preliminary Entomology field trip during July 24-30, 2017. HLC performed by MoPH staff (upper left). *An. dirus* and *An. minimus* (lower right)

Accomplishments

- Human use approval for cross-sectional blood survey obtained (July 20, 2017)
- Performed cross-sectional mass blood survey at 4 sites in August 2017
- Surat Thani province is selected as the study field site based on *Plasmodium falciparum* prevalence and ideal human population

Timeline and Cost

Activities CY	17	18	19	20
Site selection survey (cross sectional)				
Baseline surveillance (longitudinal)				
Mass Drug Administration				
Post MDA surveillance (longitudinal)				
Estimated Budget ($K)	**$507**	**$1500**	**$3000**	**$1966**

Updated: Bangkok, 29th October 2017

Goals/Milestones

CY17 – Obtain preliminary human use approvals, survey for site selection. Prepare human use protocol for longitudinal study
CY18 – Begin long-term surveillance
CY19 – Perform ivermectin MDA continue surveillance
CY20 – Continue long-term surveillance, complete data analyses

Comments/Challenges/Issues/Concerns

- Due to the unexpectedly low malaria prevalence hence the study needs to increase the size of study population. There may be no suitable antimalarial drug to be combined with ivermectin for multiple drugs MDA after the first MDA due to the exist of DHA piperaquine resistance in the GMS region. Therefore resources may be concentrated on testing the effectiveness of ivermectin MDA alone.

Budget Expenditure to Date: $507,322 USD

9. APPENDICES:

Analysis of blood survey data

- Malaria infection was defined by qMal-copies >0, Negative infection was determined from “ND” result from qMal-copies
- The prevalence was calculated as the proportion between positive malaria infection and total number of malaria tested
- There was a number of records that have missing qMal result, or ID of qMal result was not matched with survey data. These records were treated as missing value and did not included in the denominator of prevalence analysis
- Prevalence was calculated by villages, and stratified by important demographics variables, including sex, age, occupation, education, ethnicity

Table 1. The overall malaria prevalence by villages

Village	Total	Positive	Negative	Prevalence (%)
BO (Kanchanaburi)	1042	10	1032	0.96
JO (Ranong)	734	3	731	0.41
KA (Surat Thani)	790	8	782	1.01
NA (Surat Thani)	472	5	467	1.05
PA (Ranong)	617	2	615	0.32
TA (Ratchaburi)	1500	7	1493	0.47

Village BO, KA, NA had prevalence about 1%, while JO, PA, TA had prevalence <0.5

Table 2. Relationship between molecular method and RDT for malaria diagnosis

		qMAL		
		Positive	**Negative**	**Total**
RDT	**Positive**	3 (60.00)	1 (0.29)	4
	Negative	2 (40.00)	340 (99.71)	342
	Total	5 (100.00)	341 (100.00)	346

Among 345 subjects who got tested with RDT, 4 of them had positive RDT, while 5 subjects had positive for molecular method. Sensitivity of RDT = 60%, specificity 99.7%, when compared with qPCR. False positive rate for RDT = 25% (1/4), and false negative rate for RDT = 0.6% (2/341).

Table 3. Malaria prevalence stratified by demographic variables, village "BO"

Village	Total	Positive	Negative	Prevalence
BO (N)	1042	10	1032	0.0096
SEX				
Male	471 (45.20)	4 (40.00)	467 (45.25)	0.0085
Female	571 (54.80)	6 (60.00)	565 (54.75)	0.0105
Age group				
0 - 4	69 (6.64)	0 (0.00)	69 (6.71)	0.0000
5 - 10	161 (15.50)	2 (20.00)	159 (15.45)	0.0124
11 - 20	168 (16.17)	2 (20.00)	166 (16.13)	0.0119
21 - 30	154 (14.82)	1 (10.00)	153 (14.87)	0.0065
31 - 40	142 (13.67)	1 (10.00)	141 (13.70)	0.0070
41 - 50	137 (13.19)	2 (20.00)	135 (13.12)	0.0146
51 - 60	116 (11.16)	1 (10.00)	115 (11.18)	0.0086
61+	92 (8.85)	1 (10.00)	91 (8.84)	0.0109
Ethnic				
Thai	350 (33.59)	2 (20.00)	348 (33.72)	0.0057
Karen	68 (6.53)	1 (10.00)	67 (6.49)	0.0147
Burmese	615 (59.02)	7 (70.00)	608 (58.91)	0.0114
Mon	9 (0.86)	0 (0.00)	9 (0.87)	0.0000
Occupation				
Rubber tapper	8 (0.77)	0 (0.00)	8 (0.78)	0.0000
Fisherman	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Gardener	219 (21.02)	3 (30.00)	216 (20.93)	0.0137
Goverment Employee	16 (1.54)	0 (0.00)	16 (1.55)	0.0000
Merchant/Self-employed	35 (3.36)	1 (10.00)	34 (3.29)	0.0286
Logger	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
No occupation	166 (15.93)	1 (10.00)	165 (15.99)	0.0060
Student	295 (28.31)	3 (30.00)	292 (28.29)	0.0102
Other	303 (29.08)	2 (20.00)	301 (29.17)	0.0066
Body Temperature				
<37.5	1014 (97.31)	10 (100.00)	1004 (97.29)	0.0099
≥37.5	28 (2.69)	0 (0.00)	28 (2.71)	0.0000
History of Fever				
Yes	72 (6.91)	2 (20.00)	70 (6.78)	0.0278
No	970 (93.09)	8 (80.00)	962 (93.22)	0.0082

Among 10 positive case, all of them did not have fever at blood survey (BT<37.5), only 2 of them had history of having fever; 80% of positive case had asymptomatic (no history of fever).

Table 4. Malaria prevalence stratified by demographic variables, village "JO"

Village	Total	Positive	Negative	Prevalence
JO (N)	734	3	731	0.0041
SEX				
Male	366 (49.86)	0 (0.00)	366 (50.07)	0.0000
Female	368 (50.14)	3 (100.00)	365 (49.93)	0.0082
Age group				
0 - 4	33 (4.55)	0 (0.00)	33 (4.56)	0.0000
5 - 10	39 (5.37)	0 (0.00)	39 (5.39)	0.0000
11 - 20	55 (7.58)	0 (0.00)	55 (7.61)	0.0000
21 - 30	99 (13.64)	0 (0.00)	99 (13.69)	0.0000
31 - 40	120 (16.53)	1 (33.33)	119 (16.46)	0.0083
41 - 50	169 (23.28)	1 (33.33)	168 (23.24)	0.0059
51 - 60	107 (14.74)	0 (0.00)	107 (14.80)	0.0000
61+	104 (14.33)	1 (33.33)	103 (14.25)	0.0096
Ethnic				
Thai	734 (100.00)	3 (100.00)	731 (100.00)	0.0041
Karen	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Burmese	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Mon	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Occupation				
Rubber tapper	10 (1.36)	0 (0.00)	10 (1.37)	0.0000
Fisherman	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Gardener	486 (66.21)	2 (66.67)	484 (66.21)	0.0041
Goverment Employee	13 (1.77)	0 (0.00)	13 (1.78)	0.0000
Merchant/Self-employed	21 (2.86)	0 (0.00)	21 (2.87)	0.0000
Logger	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
No occupation	74 (10.08)	1 (33.33)	73 (9.99)	0.0135
Student	85 (11.58)	0 (0.00)	85 (11.63)	0.0000
Other	45 (6.13)	0 (0.00)	45 (6.16)	0.0000
Body Temperature				
<37.5	696 (94.82)	3 (100.00)	693 (94.80)	0.0043
≥37.5	38 (5.18)	0 (0.00)	38 (5.20)	0.0000
History of Fever				
Yes	70 (9.54)	0 (0.00)	70 (9.58)	0.0000
No	664 (90.46)	3 (100.00)	661 (90.42)	0.0045

Among 3 malaria positive cases, all of them were asymptomatic. All 3 positive cases were female.

Table 5. Malaria prevalence stratified by demographic variables, village "KA"

Village	Total	Positive	Negative	Prevalence
KA (N)	790	8	782	0.0101
SEX				
Male	338 (42.78)	5 (62.50)	333 (42.58)	0.0148
Female	452 (57.22)	3 (37.50)	449 (57.42)	0.0066
Age group				
0 - 4	46 (5.90)	0 (0.00)	46 (5.95)	0.0000
5 - 10	104 (13.33)	1 (14.29)	103 (13.32)	0.0096
11 - 20	78 (10.00)	1 (14.29)	77 (9.96)	0.0128
21 - 30	71 (9.10)	3 (42.86)	68 (8.80)	0.0423
31 - 40	108 (13.85)	0 (0.00)	108 (13.97)	0.0000
41 - 50	162 (20.77)	1 (14.29)	161 (20.83)	0.0062
51 - 60	128 (16.41)	1 (14.29)	127 (16.43)	0.0078
61+	83 (10.64)	0 (0.00)	83 (10.74)	0.0000
Ethnic				
Thai	790 (100.00)	8 (100.00)	782 (100.00)	0.0101
Karen	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Burmese	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Mon	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Occupation				
Rubber tapper	211 (26.71)	2 (25.00)	209 (26.73)	0.0095
Fisherman	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Gardener	266 (33.67)	4 (50.00)	262 (33.50)	0.0150
Goverment Employee	16 (2.03)	0 (0.00)	16 (2.05)	0.0000
Merchant/Self-employed	11 (1.39)	0 (0.00)	11 (1.41)	0.0000
Logger	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
No occupation	61 (7.72)	0 (0.00)	61 (7.80)	0.0000
Student	198 (25.06)	2 (25.00)	196 (25.06)	0.0101
Other	27 (3.42)	0 (0.00)	27 (3.45)	0.0000
Body Temperature				
<37.5	751 (95.06)	8 (100.00)	743 (95.01)	0.0107
≥37.5	39 (4.94)	0 (0.00)	39 (4.99)	0.0000
History of Fever				
Yes	59 (7.47)	1 (12.50)	58 (7.42)	0.0169
No	731 (92.53)	7 (87.50)	724 (92.58)	0.0096

Male were more likely to have malaria. Among 8 positive cases, all of them had BT<37.5, about 88% did not have history of fever.

Table 6. Malaria prevalence stratified by demographic variables, village "NA"

Village	Total	Positive	Negative	Prevalence
NA (N)	472	5	467	0.0106
SEX				
Male	196 (41.53)	1 (20.00)	195 (41.76)	0.0051
Female	276 (58.47)	4 (80.00)	272 (58.24)	0.0145
Age group				
0 - 4	36 (7.64)	1 (20.00)	35 (7.51)	0.0278
5 - 10	67 (14.23)	0 (0.00)	67 (14.38)	0.0000
11 - 20	62 (13.16)	0 (0.00)	62 (13.30)	0.0000
21 - 30	41 (8.70)	0 (0.00)	41 (8.80)	0.0000
31 - 40	71 (15.07)	0 (0.00)	71 (15.24)	0.0000
41 - 50	84 (17.83)	0 (0.00)	84 (18.03)	0.0000
51 - 60	59 (12.53)	0 (0.00)	59 (12.66)	0.0000
61+	51 (10.83)	4 (80.00)	47 (10.09)	0.0784
Ethnic				
Thai	472 (100.00)	5 (100.00)	467 (100.00)	0.0106
Karen	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Burmese	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Mon	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Occupation				
Rubber tapper	83 (17.58)	1 (20.00)	82 (17.56)	0.0120
Fisherman	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Gardener	191 (40.47)	2 (40.00)	189 (40.47)	0.0105
Goverment Employee	3 (0.64)	0 (0.00)	3 (0.64)	0.0000
Merchant/Self-employed	8 (1.69)	0 (0.00)	8 (1.71)	0.0000
Logger	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
No occupation	43 (9.11)	1 (20.00)	42 (8.99)	0.0233
Student	134 (28.39)	1 (20.00)	133 (28.48)	0.0075
Other	10 (2.12)	0 (0.00)	10 (2.14)	0.0000
Body Temperature				
<37.5	453 (95.97)	5 (100.00)	448 (95.93)	0.0110
≥37.5	19 (4.03)	0 (0.00)	19 (4.07)	0.0000
History of Fever				
Yes	30 (6.36)	0 (0.00)	30 (6.42)	0.0000
No	442 (93.64)	5 (100.00)	437 (93.58)	0.0113

Older people (age 61+ years) and small children (age <=4 years) were more likely to have malaria in this site (Prevalence 7.84% and 2.77%). Among 5 cases, all of them were asymptomatic.

Table 7. Malaria prevalence stratified by demographic variables, village "PA"

Village	Total	Positive	Negative	Prevalence
PA (N)	617	2	615	0.0032
SEX				
Male	310 (50.24)	2 (100.00)	308 (50.08)	0.0065
Female	307 (49.76)	0 (0.00)	307 (49.92)	0.0000
Age group				
0 - 4	25 (4.07)	0 (0.00)	25 (4.08)	0.0000
5 - 10	30 (4.89)	0 (0.00)	30 (4.90)	0.0000
11 - 20	65 (10.59)	0 (0.00)	65 (10.62)	0.0000
21 - 30	56 (9.12)	0 (0.00)	56 (9.15)	0.0000
31 - 40	106 (17.26)	0 (0.00)	106 (17.32)	0.0000
41 - 50	113 (18.40)	1 (50.00)	112 (18.30)	0.0088
51 - 60	118 (19.22)	1 (50.00)	117 (19.12)	0.0085
61+	101 (16.45)	0 (0.00)	101 (16.50)	0.0000
Ethnic				
Thai	617 (100.00)	2 (100.00)	615 (100.00)	0.0032
Karen	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Burmese	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Mon	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Occupation				
Rubber tapper	55 (8.91)	0 (0.00)	55 (8.94)	0.0000
Fisherman	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Gardener	265 (42.95)	2 (100.00)	263 (42.76)	0.0075
Goverment Employee	15 (2.43)	0 (0.00)	15 (2.44)	0.0000
Merchant/Self-employed	47 (7.62)	0 (0.00)	47 (7.64)	0.0000
Logger	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
No occupation	85 (13.78)	0 (0.00)	85 (13.82)	0.0000
Student	81 (13.13)	0 (0.00)	81 (13.17)	0.0000
Other	69 (11.18)	0 (0.00)	69 (11.22)	0.0000
Body Temperature				
<37.5	574 (93.03)	1 (50.00)	573 (93.17)	0.0017
≥37.5	43 (6.97)	1 (50.00)	42 (6.83)	0.0233
History of Fever				
Yes	55 (8.91)	1 (50.00)	54 (8.78)	0.0182
No	562 (91.09)	1 (50.00)	561 (91.22)	0.0018

Male and adult aged 41-60 years were more likely to have malaria in this village. Among 2 malaria cases, 1 of them was asymptomatic.

Table 8. Malaria prevalence stratified by demographic variables, village "TA"

Village	Total	Positive	Negative	Prevalence
TA (N)	1500	7	1493	0.0047
SEX				
Male	684 (45.60)	3 (42.86)	681 (45.61)	0.0044
Female	816 (54.40)	4 (57.14)	812 (54.39)	0.0049
Age group				
0 - 4	172 (11.49)	0 (0.00)	172 (11.54)	0.0000
5 - 10	351 (23.45)	3 (42.86)	348 (23.36)	0.0085
11 - 20	311 (20.77)	0 (0.00)	311 (20.87)	0.0000
21 - 30	153 (10.22)	1 (14.29)	152 (10.20)	0.0065
31 - 40	213 (14.23)	0 (0.00)	213 (14.30)	0.0000
41 - 50	142 (9.49)	1 (14.29)	141 (9.46)	0.0070
51 - 60	89 (5.95)	2 (28.57)	87 (5.84)	0.0225
61+	66 (4.41)	0 (0.00)	66 (4.43)	0.0000
Ethnic				
Thai	1499 (99.93)	7 (100.00)	1492 (99.93)	0.0047
Karen	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Burmese	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Mon	1 (0.07)	0 (0.00)	1 (0.07)	0.0000
Occupation				
Rubber tapper	1 (0.07)	0 (0.00)	1 (0.07)	0.0000
Fisherman	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
Gardener	162 (10.80)	1 (14.29)	161 (10.78)	0.0062
Goverment Employee	12 (0.80)	0 (0.00)	12 (0.80)	0.0000
Merchant/Self-employed	26 (1.73)	0 (0.00)	26 (1.74)	0.0000
Logger	0 (0.00)	0 (0.00)	0 (0.00)	0.0000
No occupation	406 (27.07)	3 (42.86)	403 (26.99)	0.0074
Student	597 (39.80)	2 (28.57)	595 (39.85)	0.0034
Other	296 (19.73)	1 (14.29)	295 (19.76)	0.0034
Body Temperature				
<37.5	1466 (97.73)	6 (85.71)	1460 (97.79)	0.0041
≥37.5	34 (2.27)	1 (14.29)	33 (2.21)	0.0294
History of Fever				
Yes	59 (3.93)	1 (14.29)	58 (3.88)	0.0169
No	1441 (96.07)	6 (85.71)	1435 (96.12)	0.0042

People aged 51-60 years were more likely to have malaria (Prevalence 2.29%). Among 7 malaria cases, 6 of them (86%) were asymptomatic.